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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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LEON R YANKWICH ESQ
YANKWICH & ASSOCIATES
130 BISHOP ALLEN DRIVE
CAMBRIDGE MA 02139

EXAMINER	
CHAKRABARTI,A	
ART UNIT	**PAPER NUMBER**
1655	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/353,407	Applicant(s) Lubenow et al.
	Examiner Arun Chakrabarti	Group Art Unit 1655

☒ *Responsive to communication(s) filed on* Sep 1, 2000 .

☒ *This action is* **FINAL.**

☐ *Since this application is in condition for allowance except for formal matters,* **prosecution as to the merits is closed** *in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.*

A shortened statutory period for response to this action is set to expire 3 *month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).*

Disposition of Claims

☒ *Claim(s)* 1-66 *is/are pending in the application.*

Of the above, claim(s) _____ *is/are withdrawn from consideration.*

☐ *Claim(s)* _____ *is/are allowed.*

☒ *Claim(s)* 1-66 *is/are rejected.*

☐ *Claim(s)* _____ *is/are objected to.*

☐ *Claims* _____ *are subject to restriction or election requirement.*

Application Papers

☐ *See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.*

☐ *The drawing(s) filed on* _____ *is/are objected to by the Examiner.*

☐ *The proposed drawing correction, filed on* _____ *is* ☐*approved* ☐*disapproved.*

☐ *The specification is objected to by the Examiner.*

☐ *The oath or declaration is objected to by the Examiner.*

Priority under 35 U.S.C. § 119

☐ *Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).*

☐ *All* ☐ *Some** ☐ *None of the CERTIFIED copies of the priority documents have been*

☐ *received.*

☐ *received in Application No. (Series Code/Serial Number)* _____ .

☐ *received in this national stage application from the International Bureau (PCT Rule 17.2(a)).*

**Certified copies not received:* _____ .

☐ *Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).*

Attachment(s)

☐ *Notice of References Cited, PTO-892*

☒ *Information Disclosure Statement(s), PTO-1449, Paper No(s).* 7

☐ *Interview Summary, PTO-413*

☐ *Notice of Draftsperson's Patent Drawing Review, PTO-948*

☐ *Notice of Informal Patent Application, PTO-152*

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

2. Claims 1-4,9, 13-18, 19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 are rejected under 35 U.S.C. 102 (e) as anticipated by Zhang et al. (U.S. Patent 5,942,391) (August 24, 1999).

Zhang et al teaches a method for isolating a molecule from a sample in a vessel (Example 1 and Example 9), comprising the steps of :

a) providing a multiplicity of magnetic affinity particles and incubating the particles in the presence of a detergent (Example 1, Column 27, lines 31-40, Example 9, column 39, line 56 to column 40, line 4);

b) combining the sample containing a molecule of interest with the affinity particles suitable for binding the molecule, the affinity particles being insoluble in the sample (Example 1, Column 27, lines 31-40, Example 9, column 39, line 56 to column 40, line 4);

c) immobilizing the magnetic affinity particles by applying a magnet to the vessel (Example 1, column 27, lines 42-46 and Example 9, column 40, lines 9-12);

d) separating the remainder of the sample from the immobilized magnetic affinity particles (Example 1, column 27, lines 45-46 and Example 9, column 40, lines 11-12);

e) optionally, resuspending the affinity particles in a solution (Example 1, column 27, lines 50-52 and Example 9, column 40, lines 12-18);

f) optionally, eluting the molecules from the affinity particles, followed by separating the affinity particles from the eluted molecules (Example 1, column 27, line 52 to column 28, line 29 and Example 9, column 40, lines 19-39);

wherein any of the steps b), c) ,d), e) if present, and f) if present may optionally be also performed in the presence of the detergent, wherein the use of detergent is sufficient to reduce loss of particles during any separation step (Example 1, column 27, line 52 to column 28, line 29 and Example 9, column 40, lines 19-39).

Zhang et al teaches a method wherein the combining step (a) is carried out in the absence of detergent, but detergent is added prior to the separation step (b) (Example 9, column 40, line 6).

Zhang et al teaches a method wherein the molecule of interest is selected from nucleic acids (Examples 1 and 9).

Zhang et al teaches a method wherein the particles are selected from streptavidin-coated superparamagnetic beads (Example 1, column 27, lines 37-38 to column 28, line 29 and Example 9, column 40, lines 1-2).

Zhang et al teaches a method wherein the particles are composed of materials selected from Aluminum silicates (Example 9, Column 40, line 1).

Zhang et al teaches a method wherein the nonionic detergent P-40 , a polyoxyethylene sorbitol monolaurate, is at a concentration of from about 0.0005% to 2.0% (v/v) (Example 9, column 39, line 59 and column 40, line 6).

3. Claims 1-4,9, 13-17, 20, 33-35, 44-46,48, 49 and 64-66 are rejected under 35 U.S.C. 102 (b) as anticipated by Weisburg (U.S. Patent 5,466,577) (November 14, 1995).

Weisburg teaches a method for isolating a molecule from a sample in a vessel (Example 3), comprising the steps of :

a) providing a multiplicity of magnetic affinity particles and incubating the particles in the presence of an anionic detergent SDS (Example 3, column 8, lines 1-6);

b) combining the sample containing a molecule of interest with the affinity particles suitable for binding the molecule, the affinity particles being insoluble in the sample (Example 3, column 8, lines 10-15);

c) immobilizing the magnetic affinity particles by applying a magnet to the vessel (Example 3, column 8, lines 15-19);

d) separating the remainder of the sample from the immobilized magnetic affinity particles (Example 3, column 8, lines 15-19);

e) optionally, resuspending the affinity particles in a solution (Example 3, column 8, lines 20-23);

f) optionally, eluting the molecules from the affinity particles, followed by separating the affinity particles from the eluted molecules (Example 3, column 8, lines 20-23);

wherein any of the steps b), c) ,d), e) if present, and f) if present may optionally be also performed in the presence of the detergent, wherein the use of detergent is sufficient to reduce loss of particles during any separation step (Example 3).

Weisburg teaches a method wherein the combining step (a) is carried out in the absence of detergent, but detergent is added prior to the separation step (b) (Example 3).

Weisburg teaches a method wherein the molecule of interest is selected from nucleic acids (Example 3, column 8, lines 1-2).

Weisburg teaches a method wherein the particles are selected from oligo-thymidine coated magnetic beads (Example 3, column 8, lines 10-12).

Weisburg inherently teaches a method wherein the particles are composed of materials selected from metal oxides (Example 3, column 8, lines 10-12).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-4,9, 13-17, 20, 25, 26, 33-35, 44-47,48, 49 , 56 , 57 and 64-66 are rejected under 35 U.S.C. 103 (a) in view of Weisburg (U.S. Patent 5,466,577) (November 14, 1995).

Weisburg teaches the method of claims 1-4,13-17, 20, 33-35, 44-46,48, 49 and 64-66 as described above.

Weisburg does not specify the concentration of anionic detergent in the range of .0005% to 2%.

However, it is *prima facie* obvious that selection of the specific concentration of a known detergent represents routine optimization with regard to production of desired soluble components which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art.As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the specific concentration selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

7. Claims 1-18, 19, 23, 24, 31-50, 54, 55 and 62-66 are rejected under 35 U.S.C. 103 (a) over Zhang et al. (U.S. Patent 5,942,391) (August 24, 1999) in view of McCoy et al (U.S. Patent 5,646,016) (July 8, 1997).

Zhang et al teaches the method of claims 1-4,9, 13-18, 19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 as described above.

Zhang et al does not teach a method wherein the molecule is a protein fused to metal chelating group containing six consecutive histidine residues.

McCoy et al teaches a method wherein the molecule is a protein fused to metal chelating group containing six consecutive histidine residues (Example 16, column 29, lines33-60 and column 3, line 34 to column 4, line 9).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the affinity purification using histidine patch containing fusion proteins of McCoy et al in the affinity purification method of Zhang et al since McCoy et al states, "However, the present invention provides, inter alia, the modification of a fusion partner protein, e.g., thioredoxin., in such a way as to enable it to bind to a metal chelate affinity matrix, providing an additional convenient purification tool that can be used for fusion proteins.

The technique is also applicable to other proteins, including other fusion partner proteins, and proteins which are not fusion protein constructs (column 3, lines 24-31)". McCoy et al. further provides motivation as he states, "There is provided another novel method for increasing the production of soluble recombinant proteins (column 4, lines 22-24)". An ordinary artisan would have been motivated by the express statement of McCoy to utilize the histidine patch containing fusion proteins of McCoy et al in the method of Zhang et al in order to achieve the express advantage of an improved affinity purification method with an additional convenient purification tool ,as noted by McCoy et al, which can be used for increasing the production of soluble recombinant proteins and satisfactorily purifying them..

8. . Claims 1-4, 9, 13- 19, 21, 23, 29-35, 44-50,52, 54, 55 and 60-66 are rejected under 35 U.S.C. 103 (a) over Zhang et al. (U.S. Patent 5,942,391) (August 24, 1999) in view of Gallant et al (U.S. Patent 5,798,442) (August 25, 1998).

Zhang et al teaches the method of claims 1-4, 9, 13-18, 19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 as described above.

Zhang et al does not teach the use of zwitterionic detergent 3-[cholamido-propyl)-dimethyl-ammonio]-1-propanesulfonate.

Gallant et al teaches the use of zwitterionic detergent 3-[cholamido-propyl)-dimethyl-ammonio]-1-propanesulfonate in affinity purification method (Column 22, lines 33 to column 23, line 27).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time

the invention was made to substitute the affinity purification method with suitable zwitterionic detergent of Gallant et al in the method of Zhang et al in order to separate any protein or nucleic acid from any biological sample. An ordinary artisan would have been motivated to utilize the equivalent chaotropic agents along with the affinity purification method of Gallant et al in the affinity purification method of Zhang et al in order to accomplish the considerable and satisfactory purification of proteins and nucleic acids with an useful chaotropic agents

9. Claims 1-4, 9, 13-19, 22, 27- 29, 31-35, 44-50, 52, 53- 55 and 58-66 are rejected under 35 U.S.C. 103 (a) over Zhang et al. (U.S. Patent 5,942,391) (August 24, 1999) in view of Stein et al (U.S. Patent 4,009,213) (February 22, 1977).

Zhang et al teaches the method of claims 1-4, 9, 13-18, 19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 as described above.

Zhang et al does not teach the use of cationic detergent dodecyl trimethyl ammonium chloride.

Stein et al. teaches the use of cationic detergent dodecyl trimethyl ammonium chloride. (Example 8, column 17, lines 65-67).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the suitable cationic detergent of Stein et al in the method of Zhang et al since Stein et al states, "The use of the cationic compounds is preferred in the separation of fatty alcohols of different melting points (column 6, lines 22-24)". An ordinary artisan would have been motivated by the express statement of Stein et al. to utilize

the cationic detergents of Stein et al in the method of Zhang et al in order to achieve the express advantage of a method ,as noted by Stein et al, which can be preferably used for accomplishing separation of fatty alcohols of different melting points.

Response to Arguments

10. Applicant's arguments filed on September 1, 2000, have been fully considered but they are not persuasive.

In response to applicant's argument that cited references of Zhang and Weisburg do not teach how to reduce or minimize loss of affinity particles , a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Both Zhang and Weisburg teach exactly the same structure and chemical composition of the claimed invention. Chemicals having same structure and composition inherently contains the capability of performing the intended use recited in the claims.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based

on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is no motivation to combine Zhang reference with McCoy, Gallant or Stein references. This argument is not persuasive in presence of the express motivations mentioned as follows: McCoy et al states, "However, the present invention provides, inter alia, the modification of a fusion partner protein, e.g., thioredoxin., in such a way as to enable it to bind to a metal chelate affinity matrix, providing an additional convenient purification tool that can be used for fusion proteins. The technique is also applicable to other proteins, including other fusion partner proteins, and proteins which are not fusion protein constructs (column 3, lines 24-31)". Moreover, Stein et al states, "The use of the cationic compounds is preferred in the separation of fatty alcohols of different melting points (column 6, lines 22-24)".

Applicant also argues that HPLC column method of Gallant reference is not applicable to affinity particles method of the claimed invention because it lacks some manipulative procedures of affinity particles e.g., collecting the affinity particles, separating the affinity particles with bound molecules by washing and eluting. This argument is not persuasive. An ordinary artisan with a skill in the art of biomolecule purification would have obviously practiced and substituted the manipulative procedures of affinity particles of claimed invention which are well known and routinely practiced in the art in the method of Gallant et al to achieve reasonable amount of success.

In view of the response to arguments, all rejections made in the first office action are hereby maintained.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti , Ph.D. whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Arun Kr. Chakrabarti

Arun Chakrabarti,

Patent Examiner,

September 14, 2000

JEFFREY FREDMAN
PRIMARY EXAMINER